Remarks/Arguments:

With this Response, the applicants amend claims 1 and 14 to recite a "composition comprising a spontaneous emulsion." Support is found at Page 4, lines 2-14 and throughout the specification. No new matter is added. Claims 1-30 are pending, of which, claims 1, 14, and 18 are the independent claims.

I. The Office Action

In the Acknowledgements of Remarks section of the Detailed Action, the Office Action communicates that the applicants have not amended the claims and have not argued the rejection under 35 U.S.C. § 103(a), except for the secondary reference of Li et al. The submitted Rule 132 declaration was not deemed sufficient to remove the Li et al. reference because the activity described in the Li et al. reference is activity by another before the invention by the Applicants. The Office Action suggests submitting a Rule 131 declaration may be sufficient to overcome the reference if the declaration shows that the reference describes the Applicants' own work, including one of the co-inventors not named in the Li et al. reference, namely, Dr. Kamel Egbaria. At the top of page 3, the Office Action states that the Li et al. reference was applied to show the teachings of the formulation of spontaneous emulsion with the diameter of the particles as claimed in claims 16, 17 and 28-30 and the removal of this reference would only overcome the rejection as to those claims. With this Office Action, a new reference is applied to reject those same claims.

A. Rejection under 35 U.S.C. 103(a)

The Office Action states that claims 1-30 stand rejected 35 U.S.C. § 103(a) as being unpatentable over Cho et al. (U.S. Patent 5,962,019) taken with Charman et al. (Pharmaceutical Research, Vol. 9, No. 1, pp. 87-93, 1992) and Kovacs et al. (U.S. Patent No. 5,583,105). Specifically, Cho et al. is directed to claims 1-13 and 18-26. (Page 4, second full paragraph of the Office Action). Kovacs et al. is directed to claims 1-15 and 18-27 (Page 5, second paragraph). Charman et al. is directed to claims 16, 17 and 28-30 (Page 3, first paragraph and Page 5, first paragraph).

B. The Cited References

Cho et al. is directed to a liquid and capsule form, e.g. hard and soft capsules (Col. 5, ln. 61 and 62), of an oral cyclosporin formulation of at least one alkanol solvent, a non-ionic surfactant, and a cosolvent including fatty acids and diols. The Office Action states that Cho et al. teaches an orally administered pharmaceutical composition comprising cyclosporine, ethanol, polyoxyethylene compounds, polyoxyethylene derivatives of fatty acids, an oil component, and a method of preparing a pharmaceutical formulation thereof. The Office Action

acknowledges that Cho et al. does not teach a spontaneous emulsion formulation, let alone a spontaneous emulsion having the specified diameter of particles, or the specified concentrations, or the specified ratio of components as claimed in the present invention.

Kovacs et al. is directed to an oral multiple emulsion preconcentrate of a surface active agent, ethanol and a lipophilic and/or amphiphilic solvent. Kovacs stresses the importance of having tocopheryl polyethylene glycol polycarboxylic acid esters in the formulation. Kovacs et al. states that they have "surprisingly found, that the absorption of tocopheryl polyethylene glycol polycarboxylic acid esters does not require the presence of bile acids, moreover the absorption of drugs, in our case the cyclosporin, solubilized by them is significantly improved as well." Col. 2, ln. 60-65. The preconcentrate emulsion of Kovacs et al. is to be "easily applied in the form of drink-solution and/or gelatin capsule. When the solution according to the present invention containing the active ingredient is mixed with water, tea, fruit juice, or milk (cocoa) according the patient[']s wish, a multiple emulsion (w/o/w type) forms spontaneously, without energy transfer." Col 3, ln 18-24. The Office Action states that Kovacs et al. discloses the specific and preferred concentrations and ratios as claimed and that selection of the appropriate concentrations, diameters, and ratios would have been *prima facia* obvious because where general conditions are disclosed in the prior art, it is not inventive to discover the optimal workable range (citing *In re Aller*, 220 F.2d 454 (CCPA 1995)).

Charman et al. is directed to forming a spontaneous emulsion drug delivery system (SEDDS) with a lipophilic compound, WIN 54954, in a medium chain triglyceride oil/non-ionic surfactant mixture. The chemical name of WIN 54954 is 5-(5-[2,6-dichloro-4-(4,5-dihydro-2-oxazolyl)phenoxy]-pentyl)-3-methylisoxasole. It is a methylisoxasole derivative showing specific inhibition of enteroviral replication, and is, in general, an antiviral compound.

II. Response to Examiners Acknowledgement of Remarks

For clarity of the record, the applicants respond to the Office Action refusal to consider the applicants submission of a declaration under Rule 132 to remove the Li et al. reference, even though the Office Action has supplied an additional reference if the Li et al. reference were successfully removed. The Office Action states, "the Rule 132 declaration would not overcome. . . Li et al. under 35 U.S.C. § 102(a) because the activity by another before the invention by Applicant's is applicable here." The Office Action asserts that the Li et al. reference fails to cite Dr. Egbaria and concludes that the Li et al. article is by another.

The applicants respectfully disagree. MPEP § 716.10 provides that where there is a published article identifying subject matter being claimed in an application undergoing examination, the designation of authorship or inventorship does not raise a presumption of inventorship with respect to the subject matter disclosed in the article. To rebut a rejection under 35 U.S.C. § 102(a) or (e), the inventors must provide a satisfactory showing by way of

affidavit under 37 CFR § 1.132 that the inventorship of the application is correct in that the reference discloses subject matter derived from the applicant(s) rather than invented by the author.

In this regard, page 344 of Li et al. acknowledges the advice and materials contributed by Dr. Egbaria to the subject matter of the article. Further, the applicants have submitted evidence by way of a Rule 132 declaration by Dr. Groves showing the subject matter of the Li et al. reference describes the applicants' own work, i.e., Drs. Groves and Egbaria. The applicants submit that the Li et al. reference is therefore not "by another" and therefore does not constitute prior art under 35 U.S.C. § 102(a).

The Office Action also states that the applicants should provide a Rule 131 declaration to show the reference describes applicants' own work since Dr. Egbaria was not cited in the reference. The applicants respectfully disagree with the Examiner and submit that a Rule 132 declaration is also appropriate to show Li et al. article is applicants' own work. MPEP § 715.01(c) states that the applicant may overcome the rejection by filing a specific affidavit or declaration under 37 CFR § 1.132 establishing that the article is describing applicant's own work. See also MPEP § 716.10, Example 2. The applicants therefore contend that the Rule 132 declaration by Dr. Groves was procedurally and substantively sufficient to remove the Li et al. reference from consideration, and respectfully request confirmation of this point.

III. Response to claims rejected under 35 U.S.C. § 103(a)

The Office Action presents Charman et al. in the obviousness rejection if the Li et al reference was overcome by the applicants. Because the applicants submit that the Li et al. reference has been removed, the applicants address the Office Action's alternative rejection using the Charman et al. reference.

Amended claim 1 now recites "a spontaneous emulsion of cyclosporine." The applicants agree with the Office Action that Cho et al. does not disclose a spontaneous emulsion. The applicants submit that Kovacs et al. also fails to disclose formation of a spontaneous emulsion. The Office Action cites Charman et al. as disclosing spontaneous emulsions from a lipophilic compound. Charman et al. does not disclose the specific lipophilic compound, rather, the compound is only identified by a unique identifier, WIN 54954. The applicants submit that such a bare disclosure of simply identifying a characteristic of a compound does not teach a specific compound. For example, Charman et al. is silent regarding a corticosteroid forming a spontaneous emulsion, let alone cyclosporine as claimed in amended claim 1. Although WIN 54954 is lipophilic and cyclosporine may be lipophilic, the applicants submit that such a disclosure in Charman et al. does not teach each and every limitation of the claimed invention. The applicants thus submit that because Charman et al. fails to fill the void of Cho et al. and

Kovacs et al., the combination of cited references cannot be said to render obvious the claimed invention. The Examiner's reconsideration is respectfully requested.

With regards to the rejection of the dependent claims, the Office Action submits that Cho et al. discloses various concentrations for the cyclosporine formulation. The applicants submit that if Cho et al. does not teach forming a spontaneous emulsion (as acknowledged by the April 20, 2004 Office Action at page 4), then Cho et al. can not teach the claimed ranges for such an emulsion. The Office Action also cites Kovacs et al. as disclosing the specific and preferred ranges and ratios as claimed. The Office Action states:

> Thus, the ranges disclosed in the prior art and claimed by Applicant overlap in scope, and as such, the selection of the appropriate concentrations, diameters and ratios would have been *prima facia* obvious because where the general conditions are disclosed in the prior art, it is not inventive to discover optimal workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454 (CCPA 1995).

As stated in MPEP § 2144.05, a particular parameter must first be recognized as a result-effective variable, *i.e.*, a variable which achieves a recognized result, before the determination of the optimum or workable ranges of the variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). The Office Action fails to specifically point out in the cited columns 1-4 or claims 1 and 8-12 where Kovacs et al. teaches the criticality of the present invention claimed ranges. Moreover, Kovacs et al. does not stress the ratios for the purpose of forming emulsions, but stresses the chemical stability of the composition during storage in a cool place or when dispensed into a cool liquid by adding tocopheryl polyethylene glycol polycarboxylic acid esters. Kovacs et al. is silent regarding the criticality of the claimed ranges and ratios.

Finally, the applicants specifically disagree with the Office Action characterization of the present application. The present application discusses "Neoral" and "SangCya" and their differences to the claimed invention. Nowhere in the instant application do the applicants submit that "Neoral" and "SangCya" form spontaneous emulsions. The applicants state that "Neoral" and "SangCya" are formulations of an emulsion or microemulsions, but do not state that they form spontaneous emulsions or are identified as a self-emulsifying drug delivery system (SEDDS). In this point, the applicants respectfully disagree with the Examiner's characterization of the applicant's application.

IV. Conclusion

In view of the amendments and arguments set forth above, the applicants respectfully request the Examiner's reconsideration. The applicant requests a telephonic interview with the applicant's undersigned representatives to expedite the prosecution of the application. If the claims of the application are not believed to be in full condition for allowance, for any reason, the applicants respectfully request the constructive assistance and suggestions of the Examiner in drafting one or more acceptable claims pursuant to MPEP § 707.07(j) or in making constructive suggestions pursuant to MPEP § 706.03 so that the application can be placed in allowable condition as soon as possible and without the need for further proceedings.

Respectfully submitted,

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